

WHAT IS CLAIMED:

1. A method for evaluating a physical state of a subject, which method comprises comparing (i) an expression profile of surrogate cells from the subject with (ii) a normal expression profile of surrogate cells from a normal subject or subjects, wherein a difference between the expression profiles is indicative of the physical state of the subject under investigation.
2. A method for evaluating a disease or disorder of a subject, which method comprises comparing (i) an expression profile of surrogate cells from the subject with (ii) a normal expression profile of surrogate cells from a normal subject or subjects, wherein a difference between the expression profiles is indicative of the disease or disorder of the subject under investigation.
3. The method according to claim 1, wherein the subject is a human.
4. The method according to claim 1, wherein the surrogate cells are peripheral blood leukocytes.
5. The method according to claim 4 wherein the peripheral blood leukocytes are selected from the group consisting of monocytes, macrophages, lymphocytes, granulocytes, neutrophils, basophils, and eosinophils, or other white blood cell types or subtypes.
6. The method according to claim 2, wherein the subject is a human.
7. The method according to claim 2, wherein the surrogate cells are peripheral blood leukocytes.
8. The method according to claim 7 wherein the peripheral blood leukocytes are selected from the group consisting of monocytes, macrophages, lymphocytes, granulocytes, neutrophils, basophils, and eosinophils, or other white blood cell types or subtypes.

9. The method according to claim 2, wherein the disease is the presence of a cancer in the subject.

10. The method according to claim 9, wherein the cancer is prostate cancer.

11. The method according to claim 9, wherein the cancer is breast cancer.

12. The method according to claim 2, wherein the disease is the presence of a neurological disorder.

13. The method according to claim 12, wherein the neurological disorder is a neurodegenerative disease.

14. The method according to claim 12, wherein the neurological disease is Alzheimer's disease.

15. The method according to claim 2, wherein the disorder is a psychiatric disorder or a mood disorder.

16. The method according to claim 15, wherein the disorder is schizophrenia.

17. The method according to claim 15, wherein the disorder is bipolar disorder.

18. The method according to claim 15, wherein the disorder is major depression.

19. The method according to claim 1, wherein evaluating the physical state comprises diagnosing the presence of a disease or disorder.

20. The method according to claim 1, wherein evaluating the physical state comprises determining the prognosis of the subject.

21. The method according to claim 1, wherein evaluating the physical state comprises monitoring a therapy.

22. The method according to claim 1, wherein evaluating the physical state comprises selecting a therapy.

23. The method according to claim 1, wherein evaluating the physical state comprises classifying the physical state.

24. The method according to claim 1, wherein evaluating the physical state comprises assessment of susceptibility for the physical state.

25. The method according to claim 2, wherein evaluating the disease or disorder comprises classifying the disease or disorder.

26. The method according to claim 2, wherein evaluating the disease or disorder comprises diagnosing the presence of a disease or disorder.

27. The method according to claim 2, wherein evaluating the disease or disorder comprises determining the prognosis of the subject.

28. The method according to claim 2, wherein evaluating the disease or disorder comprises monitoring a therapy.

29. The method according to claim 2, wherein evaluating the disease or disorder comprises selecting a therapy.

30. The method according to claim 2, wherein evaluating the disease or disorder comprises assessment of susceptibility for the disease or disorder.

31. The method according to claim 1, which further comprises testing for a biochemical marker of the physical state in the blood.

32. The method according to claim 1, which further comprises evaluating a biopsy tissue sample for the presence of the physical state.

33. The method according to claim 1, which comprises obtaining an expression profile on a nucleic acid microarray.

34. The method according to claim 33, wherein the microarray is an oligonucleotide microarray.

35. The method according to claim 33, wherein the microarray is a cDNA micorarray.

36. The method according to claim 1, which comprises obtaining an expression profile with reverse transcriptase-polymerase chain reaction (RT-PCR).

37. The method according to claim 2, which further comprises testing for a biochemical marker of the disease or disorder in the blood.

38. The method according to claim 2, which further comprises evaluating a biopsy tissue sample for the presence of the disease or disorder.

39. The method according to claim 2, which comprises obtaining an expression profile on a nucleic acid microarray.

40. The method according to claim 39, wherein the microarray is an oligonucleotide microarray.

41. The method according to claim 39, wherein the microarray is a cDNA micorarray.

42. The method according to claim 2, which comprises obtaining an expression profile with reverse transcriptase-polymerase chain reaction (RT-PCR).

43. A method for evaluating a physical state of a subject, which method comprises comparing an expression profile of surrogate cells from the subject with an expression profile

of surrogate cells from a known subject or subjects determined to have the physical state, wherein a similarity in the expression profiles indicates that the subject has the same physical state as the known subject.

44. A method for monitoring a physical state of a subject, which method comprises comparing an expression profile of surrogate cells from the subject with an expression profile of surrogate cells from a known subject or subjects determined to have the physical state and have a known degree of that physical state, wherein a similarity in the expression profiles indicates that the subject has a similar degree of that physical state as the known subject.

45. A method for evaluating a treatment or therapy in a subject, which method comprises comparing an expression profile of surrogate cells from the subject after the treatment or therapy with an expression profile of surrogate cells from the subject prior to treatment or therapy, wherein a difference in the expression profiles indicates an effect of the treatment or therapy on the subject.

46. The method according to claim 45, whereby the treatment is exposure to a candidate therapeutic compound.

47. A method for evaluating a treatment or therapy in a subject, which method comprises comparing the expression profile of the subject after exposing the subject to the treatment or therapy with a normal expression profile of surrogate cells from a normal subject or subjects, wherein a similarity of the expression profiles is indicative of a therapeutic benefit of the treatment or therapy on the subject.

48. The method according to claim 47, whereby the treatment is exposure to a candidate therapeutic compound.

49. A method for evaluating a treatment or therapy in a subject, which method comprises comparing the expression profile of the subject after exposing the subject to the

treatment or therapy with an expression profile of surrogate cells from other subjects with the same physical state prior to exposure to different therapies, wherein a similarity of the expression profiles is indicative of low treatment or therapy benefit on the subject.

50. The method according to claim 49, whereby the treatment is exposure to a candidate therapeutic compound.

51. A method for evaluating a treatment or therapy in a subject, which method comprises comparing the expression profile of the subject after exposing the subject to the treatment or therapy with an expression profile of surrogate cells from other subjects with the same physical state following exposure to different therapies and improvement of physical state, wherein a similarity of the expression profiles is indicative of the treatment or therapy efficacy for the subject.

52. The method according to claim 51, whereby the treatment is exposure to a candidate therapeutic compound.

53. A method for evaluating a treatment or therapy in a subject, which method comprises comparing the expression profile of the subject after exposing the subject to the treatment or therapy with an expression profile of surrogate cells from other subjects with the same physical state following exposure to different therapies and lack of improvement or worsening of the physical state, wherein a similarity of the expression profiles is indicative of a lack of treatment or therapy efficacy for the subject.

54. The method according to claim 53, whereby the treatment is exposure to a candidate therapeutic compound.

55. A method for predicting a response to treatment or therapy in a subject, which method comprises comparing an expression profile of nucleic acids from surrogate cells from the subject prior to exposing the subject to a treatment or therapy, with an expression profile of

nucleic acids from surrogate cells from other subjects with the same physical state prior to exposure to different therapies, wherein a similarity in the expression profiles predicts an effect of the treatment or therapy on the subject based on the effect of that therapy on another subject or subjects having a similar expression profile.

56. A method for choice of treatment or therapy for a subject, which method comprises comparing an expression profile of nucleic acids from surrogate cells from the subject prior to exposing the subject to a treatment or therapy with an expression profile of nucleic acids from surrogate cells from other subjects with the same physical state prior to exposure to different treatment or therapies, wherein a similarity in the expression profiles predicts an effect of the treatment or therapy on the subject based on the effect of that therapy on another subject or subjects having a similar expression profile.

57. A method for identifying a nucleic acid containing a sequence alteration that results in and/or contributes to the physical state, and/or results in and/or contributes to susceptibility for the physical state, which method comprises (a) selecting a nucleic acid that has altered expression in a surrogate cell from a subject with the physical state, when compared to a surrogate cell from a normal subject or subjects; and (b) comparing the genomic sequence of the nucleic acid, including the entire transcribed region, plus upstream and downstream controlling elements, from the subject with the physical state and the normal subject or subjects, wherein a sequence difference indicates that the nucleic acid -sequence alteration results in and/or contributes to the physical state, and/or results in and/or contributes to susceptibility for the physical state

58. The method of claim 57, wherein the nucleic acid is adjacent to, near to, or within, a region of genetic linkage to the physical state.

59. The method of claim 57, wherein the nucleic acid is genetically associated to the disease or disorder.

60. The method of claim 57 where the nucleic acid is DNA.
61. The method according to claim 57, wherein the subject is a human.
62. The method according to claim 57, wherein the surrogate cells are peripheral blood leukocytes.
63. The method according to claim 62, wherein the peripheral blood leukocytes are selected from the group consisting of monocytes, macrophages, lymphocytes, granulocytes, and eosinophils neutrophils, and basophils, or other white blood cell types or subtypes.
64. A method for identifying a nucleic acid containing a sequence alteration that results in and/or contributes to a disease or disorder, and/or results in and/or contributes to susceptibility for a disease or disorder, which method comprises (a) selecting a nucleic acid that has altered expression in a surrogate cell from a subject with the disease or disorder, when compared to a surrogate cell from a normal subject or subjects; and (b) comparing the sequence of the nucleic acid, including the entire transcribed region, plus upstream and downstream controlling elements, from the subject with disease or disorder and the normal subject or subjects, wherein a sequence difference indicates that the nucleic acid sequence results in and/or contributes to a disease or disorder, and/or results in or contributes to susceptibility for a disease or disorder.
65. The method of claim 64, wherein the nucleic acid is adjacent to, near to, or within, a region of genetic linkage to the physical state.
66. The method of claim 64, wherein the nucleic acid is genetically associated to the disease or disorder.
67. The method of claim 64 where the nucleic acid is DNA.

68. The method of claim 64, wherein the genetic alteration that is associated with a disease or disorder is indicative of the physical state of the subject.

69. The method according to claim 64, wherein the subject is a human.

70. The method according to claim 64, wherein the surrogate cells are peripheral blood leukocytes.

71. The method according to claim 64, wherein the peripheral blood leukocytes are selected from the group consisting of monocytes, macrophages, lymphocytes, granulocytes, and eosinophils neutrophils, and basophils, or other white blood cell types or subtypes.

72. The method according to claim 64, wherein the disease is the presence of a cancer in the subject.

73. The method according to claim 72, wherein the cancer is prostate cancer.

74. The method according to claim 72, wherein the cancer is breast cancer.

75. The method according to claim 64, wherein the disease is the presence of a neurological disorder.

76. The method according to claim 75, wherein the neurological disorder is a neurodegenerative disease.

77. The method according to claim 75, wherein the neurological disease is Alzheimer's disease.

78. The method according to claim 64, wherein the disorder is a psychiatric disorder or a mood disorder.

79. The method according to claim 78, wherein the disorder is schizophrenia.

80. The method according to claim 78, wherein the disorder is bipolar disorder.
81. The method according to claim 78, wherein the disorder is major depression.
82. The method according to claim 57, which further comprises testing for a biochemical marker of the physical state in the blood.
83. The method according to claim 64 which further comprises evaluating a biopsy tissue sample for the presence of said genetic alteration.
84. A method for classifying a physical state in a subject by the detection of a nucleic acid alteration in said subject, and that had previously been identified using the method of claim 57.
85. A method for diagnosing a disease or disorder in a subject by the detection of a nucleic acid alteration in said subject, wherein the nucleic acid alteration is identified using the method of claim 64.
86. A method for determining the prognosis of a subject having a disease or disorder by the detection of a nucleic acid alteration in said subject, wherein the nucleic acid alteration is identified using the method of claim 64.
87. A method for determining the susceptibility of a subject for a physical state by the detection of a nucleic acid alteration in said subject, wherein the nucleic acid alteration is identified using the method of claim 57.
88. A method for determining the susceptibility of a subject for developing a disease or disorder by the detection of a nucleic acid alteration in said subject, wherein the nucleic acid alteration is identified using the method of claim 64.

89. A method for developing therapeutic compounds to be administered to a subject with a physical state resulting from and/or contributed to, by a nucleic acid sequence alteration identified by the method of claim 57, whereby the therapeutic compounds are designed to normalize the function or expression of the altered nucleic sequence.

90. A method for developing therapeutic compounds to be administered to a subject with a disease or disorder resulting from and/or contributed to, by a nucleic acid sequence alteration identified by the method of claim 64, whereby the therapeutic compounds are designed to normalize the function or expression of the altered nucleic sequence.

91. A method for treating a subject with a physical state resulting from and/or contributed to, by a nucleic acid sequence alteration identified by the method of claim 57, comprising administering to a subject in need of such treatment therapeutically effective amounts of a normal counterpart of the nucleic acid sequence.

92. The method of claim 91, wherein said nucleic acid is administered with a viral vector.

93. A method for treating a patient suffering from a disease or a disorder resulting from and/or contributed to, by a nucleic acid sequence alteration that had been previously identified using the method of claim 64, comprising administering to a patient in need of such treatment therapeutically effective amounts of a normal counterpart of the nucleic acid sequence.

94. The method of claim 93, wherein said nucleic acid is administered with a viral vector.

95. A method for treating a subject with a physical state resulting from and/or contributed to, by an altered expression level of a nucleic acid identified to have altered

expression using the method of claim 1, comprising administering to a subject in need of such treatment therapeutically effective amounts of the nucleic acid.

96. The method of claim 95, wherein said nucleic acid is administered with a viral vector.

97. A method for treating a subject with a disease or disorder resulting from and/or contributed to, by an altered expression level of a nucleic acid identified to have altered expression using the method of claim 2, comprising administering to a subject in need of such treatment therapeutically effective amounts of the nucleic acid.

98. The method of claim 97, wherein said nucleic acid is administered with a viral vector.

99. A method for treating a subject with a physical state resulting from and/or contributed to, by an altered expression level of a nucleic acid identified to have altered expression using the method of claim 1, comprising administering to a subject in need of such treatment therapeutically effective amounts of inhibitory nucleic acid sequence specific for the nucleic acid.

100. The method of claim 99, wherein said nucleic acid is administered with a viral vector.

101. A method for treating a subject with a disease or disorder resulting from and/or contributed to, by an altered expression level of a nucleic acid identified to have altered expression using the method of claim 2, comprising administering to a subject in need of such treatment therapeutically effective amounts of inhibitory nucleic acid sequence specific for the nucleic acid.

102. The method of claim 101, wherein said nucleic acid is administered with a viral vector.

103. A method for developing therapeutic compounds for a physical state resulting from and/or contributed to, by an altered expression level of a nucleic acid identified to have altered expression using the method of claim 1, whereby the therapy is designed to normalize the function or expression of the nucleic sequence.

104. A method for developing therapeutic compounds for a disease or disorder resulting from and/or contributed to, by an altered expression level of a nucleic acid identified to have altered expression using the method of claim 2, whereby the therapy is designed to normalize the function or expression of the nucleic sequence.